

BEST AVAILABLE COPY

May-19-06 01:30pm From-HBS&R

1978-341-0136

T-679 P.06/31 F-558

10/729,427

- 2 -

Amendments to the Claims

Please amend Claims 1 and 14 to correct typographical errors.

Please cancel Claims 25-55. Applicants reserve the right to file a continuing application or take such other appropriate action as deemed necessary to protect the non-elected inventions. Applicants do not hereby abandon or waive any rights in the non-elected inventions.

Rejoinder of Claims 5-9, 16-19 and 24, withdrawn in response to the requirement for the election of species, is hereby requested.

The Claim Listing below will replace all prior versions of the claims in the application:

Claim Listing

1. (Currently Amended) A method of treating a patient suffering from an inflammatory condition, comprising
treating said patient with a therapeutically effective amount of a cholinergic agonist selective for an $\alpha 7$ nicotinic receptor,
wherein said condition is selected from the group consisting of appendicitis, peptic, gastric and duodenal ulcers, peritonitis, pancreatitis, epiglottitis, achalasia, cholangitis, cholecystitis, hepatitis, Whipple's disease, asthma, allergy, anaphylactic shock, immune complex disease, organ ischemia, reperfusion injury, organ necrosis, hay fever, sepsis, septicemia, endotoxic shock, cachexia, hyperpyrexia, eosinophilic granuloma, granulomatosis, sarcoidosis, septic abortion, epididymitis, vaginitis, prostatitis, urethritis, bronchitis, emphysema, rhinitis, cystic fibrosis, pneumonitis, pneumoultramicroscopic silicovolcanoconiosis, alveitis, bronchiolitis, pharyngitis, pleurisy, sinusitis, influenza, respiratory syncytial virus infection, herpes infection, HIV infection, hepatitis B virus infection, hepatitis C virus infection, disseminated bacteremia, Dengue fever, candidiasis, malaria, filariasis, amebiasis, hydatid cysts, burns, vasulitis, angitis, endocarditis, arteritis, atherosclerosis, thrombophlebitis, pericarditis, myocarditis, myocardial ischemia, periarthritis nodosa, rheumatic fever, coeliac disease, congestive heart failure, adult respiratory distress syndrome, chronic obstructive pulmonary disease, meningitis, encephalitis, neuritis, neuralgia, spinal cord injury,

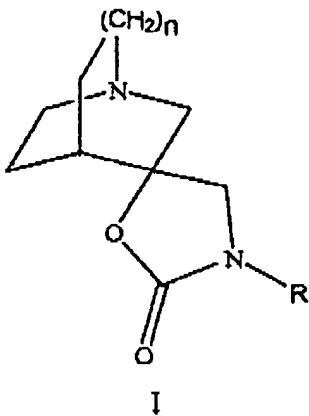
10/729,427

- 3 -

paralysis, uveitis, arthritides, arthralgias, osteomyelitis, fasciitis, Paget's disease, gout, periodontal disease, rheumatoid arthritis, synovitis, myasthenia gravis, thryoiditis, systemic lupus erythematosus, Goodpasture's syndrome, Behcets's syndrome, allograft rejection, graft-versus-host disease, ~~ankylosing spondylitis, Berger's disease, ankylosing spondylitis, Berger's disease, Retier's syndrome, and Hodgkins disease.~~

2-3. (Cancelled)

4. (Original) The method of claim 1, wherein the cholinergic agonist is selected from the group consisting of a quaternary analog of cocaine; (1-aza-bicyclo[2.2.2]oct-3-yl)-carbamic acid 1-(2-fluorophenyl)-ethyl ester; a compound of formula I:

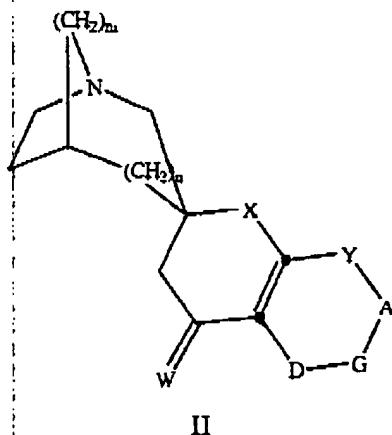


wherein, R represents hydrogen or methyl, and

n represents 0 or 1; a pharmaceutically acceptable salt of a compound of formula I; a compound of formula II:

10/729,427

- 4 -



wherein:

m is 1 or 2,

n is 0 or 1,

Y is CH, N or NO,

X is oxygen or sulfur,

W is oxygen, H₂ or F₂,A is N or C(R²),G is N or C(R³),D is N or C(R⁴),

with the proviso that no more than one of A, G and D is nitrogen but at least one of Y, A, G and D is nitrogen or NO,

R¹ is hydrogen or C₁-C₄ alkyl,

R², R³ and R⁴ are independently hydrogen, halogen, C₁-C₄ alkyl, C₂-C₄ alkenyl, C₂-C₄ alkynyl, aryl, heteroaryl, OH, OC₁-C₄ alkyl, CO₂R₁, -CN, -NO₂, -NR₅R₆, -CF₃ or -OSO₂CF₃, or R² and R³, R³ and R⁴, respectively, may together form another six membered aromatic or heteroaromatic ring sharing A and G, or G and D, respectively, containing between zero and two nitrogen atoms, and substituted with one to two of the following substituents: independently hydrogen, halogen, C₁-C₄ alkyl, C₂-C₄ alkenyl, C₂-C₄ alkynyl, aryl, heteroaryl, OH, OC₁-C₄ alkyl, CO₂R¹, -CN, -NO₂, -NR⁵R⁶, -CF₃ or -OSO₂CF₃,

10/729,427

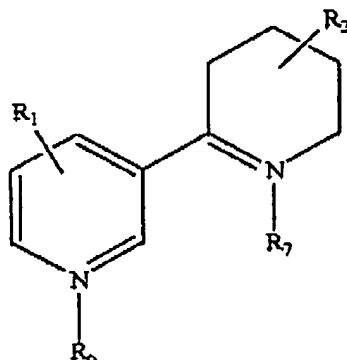
- 5 -

R^5 and R^6 are independently hydrogen, C_1 - C_4 alkyl, $C(O)R^7$, $C(O)NHR^8$, $C(O)OR^9$, SO_2R^{10} or may together be $(CH_2)_jQ(CH_2)_k$ where Q is O, S, NR^{11} , or a bond,

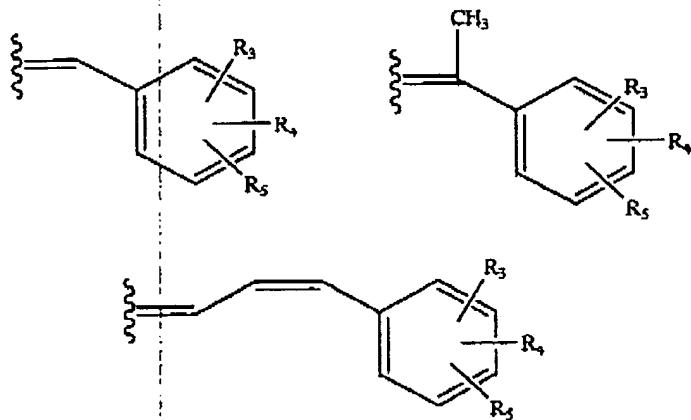
j is 2 to 7,

k is 0 to 2,

R^7 , R^8 , R^9 , R^{10} and R^{11} are independently C_1 - C_4 alkyl, aryl, or heteroaryl, or an enantiomer thereof; a pharmaceutically acceptable salt of a compound of formula II; a compound of formula III:



wherein R_1 , R_6 and R_7 are hydrogen or C_1 - C_4 alkyl, and R_2 is selected from a group of

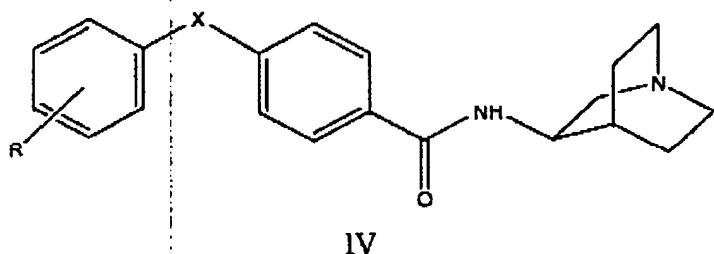


and

10/729,427

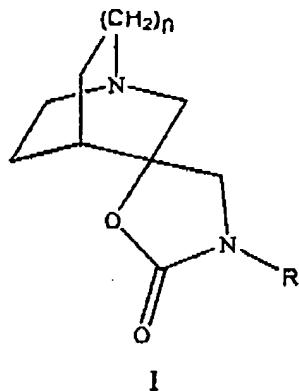
- 6 -

wherein, R₃, R₄ and R₅ are selected from the group consisting of hydrogen, C₁-C₄ alkyl optionally substituted with N,N-dialkylamino having 1 to 4 carbons in each of the alkyls, C₁-C₆ alkoxy optionally substituted with N,N-dialkylamino having 1 to 4 carbons in each of the alkyls, carboalkoxy having 1 to 4 carbons in the alkoxy, amino, amido having 1 to 4 carbons in the acyl, cyano, and N,N-dialkylamino having 1 to 4 carbons in each of the alkyls, halo, hydroxyl or nitro; and a compound of formula IV:



wherein X is O or S, and R is selected from the group consisting of H, OR₁, NHC(O)R₁, and a halogen, wherein R₁ is a C₁-C₄ alkyl.

5. (Original) The method of claim 1, wherein the cholinergic agonist is a compound of formula I:

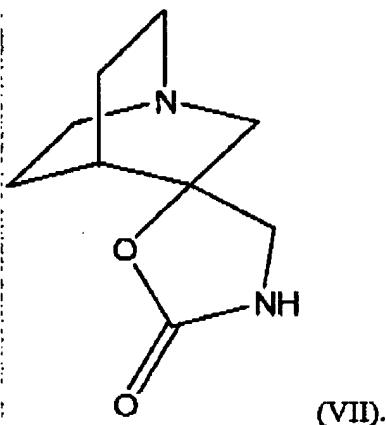


wherein, R represents hydrogen or methyl, and n represents 0 or 1;
or a pharmaceutically acceptable salt thereof.

10/729,427

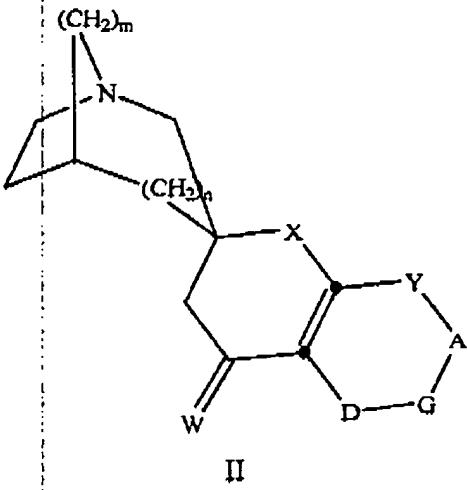
- 7 -

6. (Original) The method of claim 5, wherein the cholinergic agonist is (-)-spiro[1-azabicyclo[2.2.2]octane-3,5'-oxazolidin-2'-one]



(VII).

7. (Original) The method of claim 1, wherein the cholinergic agonist is a compound of formula II:



II

wherein:

m is 1 or 2;

n is 0 or 1;

Y is CH, N or NO;

X is oxygen or sulfur;

W is oxygen, H2 or F2;

A is N or C(R²);

10/729,427

- 8 -

G is N or C(R³);D is N or C(R⁴);

with the proviso that no more than one of A, G and D is nitrogen but at least one of Y, A, G and D is nitrogen or NO;

R¹ is hydrogen or C₁-C₄ alkyl;

R², R³ and R⁴ are independently hydrogen, halogen, C₁-C₄ alkyl, C₂-C₄ alkenyl, C₂-C₄ alkynyl, aryl, heteroaryl, OH, OC₁-C₄ alkyl, CO₂R₁, -CN, -NO₂, -NR₅R₆, -CF₃ or -OSO₂CF₃, or R² and R³, R³ and R⁴, respectively, may together form another six membered aromatic or heteroaromatic ring sharing A and G, or G and D, respectively, containing between zero and two nitrogen atoms, and substituted with one to two of the following substituents: independently hydrogen, halogen, C₁-C₄ alkyl, C₂-C₄ alkenyl, C₂-C₄ alkynyl, aryl, heteroaryl, OH, OC₁-C₄ alkyl, CO₂R¹, -CN, -NO₂, -NR⁵R⁶, -CF₃ or -OSO₂CF₃;

R⁵ and R⁶ are independently hydrogen, C₁-C₄ alkyl, C(O)R⁷, C(O)NHR⁸, C(O)OR⁹, SO₂R¹⁰ or may together be (CH₂)_jQ(CH₂)_k where Q is O, S, NR¹¹, or a bond;

j is 2 to 7;

k is 0 to 2;

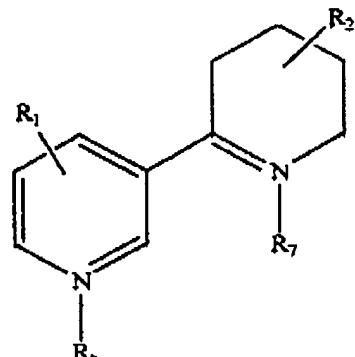
R⁷, R⁸, R⁹, R¹⁰ and R¹¹ are independently C₁-C₄ alkyl, aryl, or heteroaryl, or an enantiomer thereof, or a pharmaceutically acceptable salts thereof.

8. (Original) The method of claim 7, wherein the cholinergic agonist is a compound of formula II wherein m is 1; n is 0; p is 0; x is oxygen; A is C(R²); G is C(R³); and D is C(R⁴).
9. (Original) The method of claim 7, wherein the cholinergic agonist is 5'-phenylspiro[1-azabicyclo[2.2.2]octane-3,2'-(3'H)-furo[2,3-b]pyridin].

10/729,427

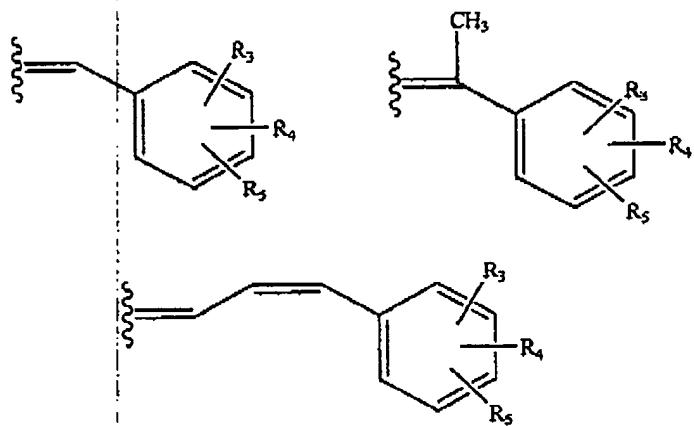
- 9 -

10. (Original) The method of claim 1, wherein the cholinergic agonist is a compound of formula III:



(III)

wherein R₁, R₆ and R₇ are hydrogen or C₁-C₄ alkyl; and R₂ is selected from a group of



and wherein, R₃, R₄ and R₅ are selected from the group consisting of hydrogen, C₁-C₄ alkyl optionally substituted with N,N-dialkylamino having 1 to 4 carbons in each of the alkyls, C₁-C₆ alkoxy optionally substituted with N,N-dialkylamino having 1 to 4 carbons in each of the alkyls, carboalkoxy having 1 to 4 carbons in the alkoxy, amino, amido having 1 to 4 carbons in the acyl, cyano, and N,N-dialkylamino having 1 to 4 carbons in each of the alkyls, halo, hydroxyl or nitro.

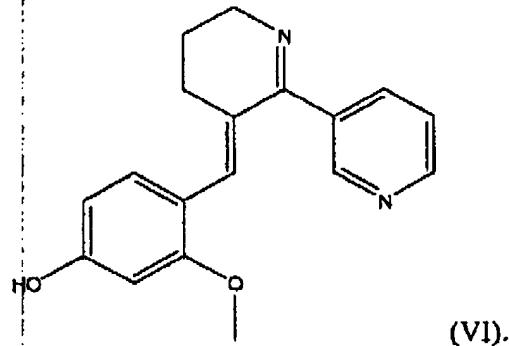
10/729,427

- 10 -

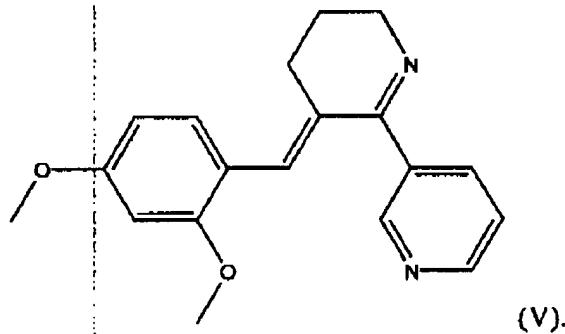
11. (Original) The method of claim 10, wherein the cholinergic agonist is a compound of formula III, wherein R₂ is attached to the 3-position of the tetrahydropyridine ring, and further wherein R₃, which is attached to the 4- or the 2- position of the phenyl ring, is selected from the group consisting of amino, hydroxyl, chloro, cyano, dimethylamino, methyl, methoxy, acetylamino, acetoxy, and nitro.
12. (Original) The method of claim 10, wherein the cholinergic agonist is a compound selected from the group consisting of formula III, wherein R₃ is hydroxyl, and wherein R₁, R₄, and R₅ are hydrogen; formula III, wherein R₃ is acetylamino and wherein R₁, R₄, and R₅ are hydrogen; formula III, wherein R₃ is acetoxy and wherein R₁, R₄, and R₅ are hydrogen; formula III, wherein R₃ is methoxy, and wherein R₁, R₄, and R₅ are hydrogen; formula III, wherein R₃ is methoxy and wherein R₁ and R₄ are hydrogen, and further wherein R₃ is attached to the 2-position of the phenyl ring, and R₅, which is attached to the 4-position of the phenyl ring, is methoxy or hydroxy.
13. (Original) The method of claim 10, wherein the cholinergic agonist is selected from the group consisting of 3-(2,4-dimethoxybenzylidene)anabaseine (DMXB-A), 3-(4-hydroxybenzylidene)anabaseine, 3-(4-methoxybenzylidene)anabaseine, 3-(4-aminobenzylidene)anabaseine, 3-(4-hydroxy-2-methoxybenzylidene)anabaseine, 3-(4-methoxy-2-hydroxybenzylidene)anabaseine, trans-3-cinnamylidene anabaseine, trans-3-(2-methoxy-cinnamylidene)anabaseine and trans-3-(4-methoxycinnamylidene)anabaseine.
14. (Currently Amended) The method of claim 10, wherein the cholinergic agonist is 3-(4-hydroxy-2-methoxybenzylidene) anabasine anabaseine

10/729,427

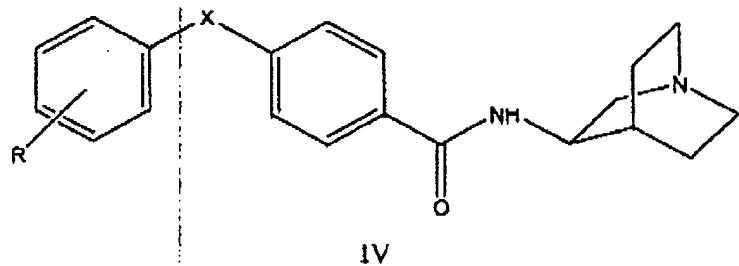
- 11 -



15. (Original) The method of claim 10, wherein the cholinergic agonist is 3-(2,4-dimethoxybenzylidene)anabaseine.



16. (Original) The method of claim 1, wherein the cholinergic agonist is a compound of formula IV:



wherein X is O or S; and

R is selected from the group consisting of H, OR₁, NHC(O)R₁, and a halogen, wherein R₁ is a C₁-C₄ alkyl.

10/729,427

- 12 -

17. (Original) The method of claim 15, wherein the cholinergic agonist is selected from a group consisting of N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-4-(4-hydroxyphenoxy)benzamide, N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-4-(4-acetamidophenoxy)benzamide, N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-4-(phenylsulfanyl)benzamide, and N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-4-(3-chlorophenylsulphonyl)benzamide.
18. (Original) The method of claim 15, wherein the cholinergic agonist is N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-4-(phenylsulfanyl)benzamide.
19. (Original) The method of claim 1, wherein the cholinergic agonist is cocaine methiodide.
20. (Original) The method of claim 1 wherein the condition is selected from the group consisting of appendicitis, peptic, gastric and duodenal ulcers, peritonitis, pancreatitis, hepatitis, asthma, allergy, anaphylactic shock, organ necrosis, hay fever, sepsis, septicemia, endotoxic shock, cachexia, septic abortion, disseminated bacteremia, burns, coeliac disease, congestive heart failure, adult respiratory distress syndrome, chronic obstructive pulmonary disease, rheumatoid arthritis, systemic lupus erythematosis, myocardial ischemia, spinal cord injury, paralysis, allograft rejection and graft-versus-host disease.
21. (Original) The method of claim 1 wherein the condition selected from the group consisting of appendicitis, peptic, gastric or duodenal ulcers, peritonitis, pancreatitis, hepatitis, asthma, allergy, anaphylactic shock, organ necrosis, hay fever, sepsis, septicemia, endotoxic shock, cachexia, septic abortion, disseminated bacteremia, burns, congestive heart failure, adult respiratory distress syndrome, chronic obstructive pulmonary disease, rheumatoid arthritis, systemic lupus erythematosis, myocardial ischemia, cerebral infarction, cerebral embolism, spinal cord injury, paralysis, allograft rejection or graft-versus-host disease.
22. (Original) The method of Claim 1 wherein the condition is selected from the group consisting of peritonitis, pancreatitis, sepsis, endotoxic shock, adult respiratory distress

10/729,427

- 13 -

syndrome, chronic obstructive pulmonary disease, rheumatoid arthritis, systemic lupus erythematosis, myocardial ischemia, allograft rejection, asthma, graft-versus-host-disease, congestive heart failure and cystic fibrosis.

23. (Original) The method of claim 1, wherein the condition selected from the group consisting of peritonitis, pancreatitis, sepsis, endotoxic shock, cachexia, adult respiratory distress syndrome, chronic obstructive pulmonary disease, rheumatoid arthritis, systemic lupus erythematosis, myocardial ischemia, and allograft rejection.
24. (Original) The method of claim 1, wherein the condition is sepsis.
- 25-55. (Cancelled)

**This Page is Inserted by IFW Indexing and Scanning
Operations and is not part of the Official Record**

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

BLACK BORDERS

IMAGE CUT OFF AT TOP, BOTTOM OR SIDES

FADED TEXT OR DRAWING

BLURRED OR ILLEGIBLE TEXT OR DRAWING

SKEWED/SLANTED IMAGES

COLOR OR BLACK AND WHITE PHOTOGRAPHS

GRAY SCALE DOCUMENTS

LINES OR MARKS ON ORIGINAL DOCUMENT

REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY

OTHER: _____

IMAGES ARE BEST AVAILABLE COPY.

As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.